REMARKS

Claims 1, 2, 5, 6-14, 17, 42, 45-47 and 51-65 are pending. Claims 3, 4, 15, 16, 18-41, 43, 44 and 48-50 are canceled as a consequence of the restriction requirement and without prejudice to the prosecution of their subject matter in other patent applications. New claims 51-65 are added, and are based on the original claims, and do not contain new matter. Claim 17 is deleted so that it is no longer redundant over claim 12. The amendment of claim 12 is supported by the instant specification at paragraph 91, and does not constitute new matter.

With regard to the restriction requirement, Applicants thank the Examiner for agreeing to join group 25 with elected group 12. Because election of group 25 would have triggered a species election of 'cargo,' now that group 25 is under consideration, Applicants elect the species, "therapeutic proteins."

The claims are amended to delete subject matter no longer being pursued as a result of the restriction requirement. These amendments are made without prejudice to the prosecution of the subject matter in other patent applications.

1. The Claim Objections Are Addressed By Amendment

Claims 1, 2, 5, 6-14, 17, 42 and 45-47 (in part) are objected to because the claims recite non-elected subject matter. Claims 12 and 17 are objected to because both claims 12 and 17 have the same language and are both dependent on claim 6.

The claims have been amended to delete non-elected subject matter. Claim 17 is deleted, so that it is no longer redundant over claim 12.

For the above reasons, the objections to the claims should be withdrawn.

2. The Claims Are Not Anticipated By Anderson

Claims 1, 2, 5, 6-11, 13, 42 and 45-47 (in part) are rejected under 35 U.S.C. §102(b) as anticipated by European Patent Application Publication No. 0 359 347 by NeoRx, inventors Anderson et al.. According to the Examiner, Anderson teaches covalently-linked complexes ("CLCs") for targeting a defined population of cells which comprise a targeting peptide and a cytotoxic agent. The Examiner states:

> The reference teaches that peptides or analogs that include a sequence present in the highly basic region, such as CFITKALGISYGRKK**RRQRR**RPPQGS . . . are conjugated to targeting protein conjugates to aid in internalization and targeting to the nucleus

where underlined and bolded **RRQRR** is SEQ ID NO:97 of the claims. Based on this teaching, the Examiner contends that Anderson anticipates the claims.

Applicants assert that Anderson does not anticipate the amended claims. The claims have been amended so that RRQRR (SEQ ID NO:97) is no longer recited in claims 1, 6 or 42, but rather is provided for in new claims 51-65, in which RRQRR is either an isolated peptide or part of a peptide-cargo complex wherein the peptide *is* RRQRR. Therefore, Anderson does not anticipate the claims relating to SEQ ID NO:97. Applicants respectfully request that the rejection be withdrawn.

3. The Claims Are Not Anticipated By Barsoum

Claims 1, 2, 5, 6-11, 42 and 45-47 (in part) are rejected under 35 U.S.C. §102(b) as being anticipated by European Patent Application Publication No. 0 656 950 by Biogen, Inc., inventors Barsoum et al. ("Barsoum"). The Examiner states that

Barsoum teaches intracellular delivery of cargo molecules by transport peptides, including Tat-derived sequences that contain an RRQRR sequence, and the Examiner contends that Barsoum anticipates the claims.

Applicants assert that Barsoum does not anticipate the amended claims. The claims have been amended so that RRQRR (SEQ ID NO:97) is no longer recited in claims 1, 6 or 42, but rather is provided for in new claims 51-65, in which RRQRR is either an isolated peptide or part of a peptide-cargo complex wherein the peptide *is* RRQRR. Therefore, Barsoum does not anticipate the claims relating to SEQ ID NO:97. Applicants respectfully request that the rejection be withdrawn.

4. The Claims Are Not Anticipated By Vivès

Claims 1, 2, 5, 6-7, 9-11, 42 and 45-47 (in part) are rejected under 35 U.S.C. §102(b) as anticipated by Vivès et al., 1997, Letters in Peptide Science 4:429-436 ("Vivès").

The Examiner states that Vivès teaches that peptide 37-72 from HIV tat allows internalization of conjugated proteins, and teaches various modified peptides which contain an RRQRR sequence. The Examiner contends that Vivès anticipates the claims.

Applicants assert that Vivès does not anticipate the amended claims. The claims have been amended so that RRQRR (SEQ ID NO:97) is no longer recited in claims 1, 6 or 42, but rather is provided for in new claims 51-65, in which RRQRR is either an isolated peptide or part of a peptide-cargo complex wherein the peptide *is* RRQRR. Therefore, Vivès does not anticipate the claims relating to SEQ ID NO:97. Applicants respectfully request that the rejection be withdrawn.

5. The Claims Are Not Obvious

Claims (1, 2, 5, 6-14, 17, 42 and 45-47 in part) are rejected under 35 U.S.C. §103(a) as obvious over either Anderson, Barsoum, or Vivès and United States Patent No. 6,287,792 by Pardridge et al. ("Pardridge").

The Examiner contends that where Anderson, Barsoum, and Vivès teach RRQRR-containing peptides, Pardridge teaches compositions for delivering an agent into cells or organisms, where the compositions comprise either avidin or an avidin fusion protein as a transporter vector bonded to a biotinylated agent to form an avidin-biotin-agent complex. The Examiner states:

> Thus, it would have been obvious to one skilled in the art at the time the invention was made to use the avidin-biotin as labeling or linking molecules to the peptide-cargo complexes of the instant invention, since Pardridge et al. teach the advantages of linking the peptides to biotin and then link [*sic*] the avidin labeled peptides to use as transporter vectors. A person skilled in the art would have been motivated to use the avidin-biotin bond since it has the highest affinity binding reactions, and the biotin-avidin bond is most stable in serum and in circulation, such that drugs can be targeted and delivered to the target tissue to produce pharmacological activity.

Applicants respectfully disagree, and assert that the claims are not obvious. First, it should be noted that the above rejection would not apply to any of claims 1, 2, 5, 6-14, 42 or 45-47, as these claims no longer contain SEQ ID NO:97.

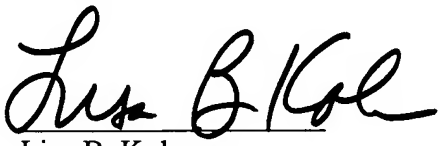
As regards new claims 51-65, Applicants assert that none of these claims are obvious over any one of Anderson, Barsoum, Vivès or Pardridge, or any combination thereof. None of these references disclose that RRQRR can be separated from the sequences in which it is embedded and retain transport activity. To the contrary, Vivès

teaches that retention of ALL basic amino acids in Tat peptide 48-60 is important to transport activity, whereas RRQRR (SEQ ID NO:97) lacks two of six arginine residues. Accordingly, the skilled artisan would not have reasonably expected that RRQRR itself could be successfully used to transport cargo. Therefore, the cited references do not convey the requisite reasonable expectation of success, and cannot, singly or in combination, render the claims obvious. Applicants respectfully request that the rejection be withdrawn.

6. Conclusion

For all the foregoing reasons, it is earnestly requested that the rejection be withdrawn and that the claims be allowed to issue.

Respectfully submitted,



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